UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,614	05/08/2001	Yashwant M. Deo	MXI-166	4957

959 7590 11/03/2004

LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,614	DEO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-78* is/are pending in the application.

4a) Of the above claim(s) *72-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *56-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, Claims 56-71, without traverse, in the paper filed 8/13/04, is acknowledged.

2. Claims 72-78 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 56-71 are being acted upon.

3. In view of the papers filed 7/19/04, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48 (a). The inventorship of this application has been changed by the addition of Inventor John Treml.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 56-63, 70, and 71, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) In Claim 56, "that" in line 5 of the claim should properly be "than"; in part (e) the phrase "enhances the presentation of the antigen" is vague and indefinite as the comparative phrase does not recite what antigen presentation is enhanced in comparison to.

B) In Claim 70, V_H 5-51 and V_k L15 comprise vague and indefinite terms - in the given context they appear to comprise undefined laboratory designations; the recitation of an antibody comprising genes is nonsensical as an antibody is a protein and genes are DNA, thus, an antibody cannot comprise a gene.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 56-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the antibody designated B11 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. A deposit may be made under the provisions of the Budapest Treaty; an affidavit or declaration to that effect is required. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, Applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a U.S. patent.

Applicant's deposit and provision of these assurances through the submission of an appropriate declaration would obviate this rejection.

8. Claims 56-71 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) An isolated human monoclonal antibody, or an antigen-binding portion thereof, that has the following properties:

a) the antibody binds to human dendritic cells:

b) the antibody binds to human macrophages but to a lesser extent that the binding to human dendritic cells;

c) the antibody inhibits dextran uptake by human dendritic cells;

d) the antibody is internalized following binding to human dendritic cells; and

e) the antibody, when conjugated to an antigen, enhances presentation of the antigen by human dendritic cells (Claim 56).

B) Claims 57-63 and 70 which depend from Claim 56; additionally,

C) The antibody of Claim 56 ... with a binding affinity of at least about 10^8 M^{-1} (Claim 61).

D) The antibody of Claim 56 ... which is an antibody fragment (Claim 63).

E) Claims 67-70 which comprise antibodies comprising portions of the V_L and V_H regions of SEQ ID NOS:2 and 4 respectively.

F) An isolated antibody comprising ... V_H 5-51 and V_k L15 (Claim 70).

Applicant's amendment, filed 10/07/03, asserts that support for the new limitations can be found at various sites throughout the specification. As set forth below, however, support for the aforementioned specific limitations has not been found.

Regarding A) and B), Applicant indicates that support for the limitations of the claims can be found generally in Example 2. Example 2 describes the results of the characterization of the B11 antibody. Said characterization of a single antibody is insufficient support for the generic claims encompassing any antibody that might comprise the recited properties or characteristics.

Also note that while the specification discloses a generic human antibody that binds dendritic cells, it does not disclose, and cannot support, a generic antibody that binds *human* dendritic cells.

Regarding C), the specific binding affinity, 10^8 M^{-1}, is not disclosed in the specification.

Regarding D), the specification discloses fragments of an "antigen-binding portion of an antibody" or "binding fragments", but not the more generic "fragments".

Regarding E), Applicant asserts that antibodies comprising various subsequences of SEQ ID NOS:2 and 4, e.g., an antibody comprising only the CDR3's (Claim 64), are supported by the complete sequences. Applicant is advised that the disclosure of a genus (SEQ ID NOS:2 and 4) is insufficient support for claims

drawn to a subgenus (the CDR fragments of SEQ ID NOS:2 and 4). Even regarding Claim 68, wherein the entire SEQ ID NOS:2 and 4 are recited, the specification cannot support antibodies comprising *any* other constant regions.

Regarding F), V_H 5-51 and V_k L15 are not disclosed in the specification.

9. Claims 56-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of:

A) An isolated human monoclonal antibody comprising the functional limitations of Claims 56-63, except the B11 antibody, nor any fragments thereof.

B) An isolated human monoclonal antibody comprising conservative modifications of the antibodies of Claims 64-66.

C) An isolated human monoclonal antibody at least 80% homologous to the antibody of Claims 67.

Regarding A), the specification discloses just a single example (species) of the claimed genus of antibodies (B11); no fragments are disclosed. Regarding B) and C), no examples are disclosed. Accordingly, in its entirety, the specification discloses just a single example of several essentially unlimited genuses. Given the essentially unlimited number of antibodies encompassed by the claims, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genuses. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

10. Claims 63-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable.

Given the established unpredictability of the art, the instant specification would require a significant teaching to be enabled. In particular, it is unlikely that the antibody fragments, conservatively modified antibodies, or 80% homologous antibodies encompassed by the claims could function for their intended use. Note that the fragments and antibodies of the claims would encompass fragments and antibodies modified in the CDR binding regions of the antibodies. It is well-established that even a single substitution in the CDR regions of an antibody can have a dramatic, and unpredictable, effect on antibody binding (and thus, function). See, for example, Kobayashi et al. (1999) wherein it is taught that even single conserved substitutions can have a large effect on antibody binding (see Figure 4; note the log scale). Note the breadth of the claims; the fragments and modified antibodies of the claims are not limited in the number of modifications/substitutions allowed. Thus, even antibodies in which *all* of the amino acids are changed would be encompassed by the claims.

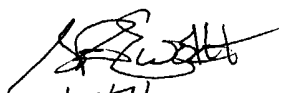
The instant specification provides no examples of the fragments or modified antibodies of the instant claims. Accordingly, one of ordinary skill in the art must conclude that the specification fails to adequately disclose how to make and use the claimed invention. Thus, the invention is considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

11. No claim is allowed.

12. The references of the IDS's filed 2/22/02 and 7/01/02 have not been received. The U.S. Patents and some of the WO documents of the IDS's are available and have been initialed on the Form 1449's.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

14. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



10/27/04

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600